FOOD AND DRUG ADMINISTRATION

CENTER FOR BIOLOGICS EVALUATION AND RESEARCH

MEMORANDUM

DATE: **June 4, 2007**

FROM: **Stephany J. Wesley, Chief, Blood and Tissue Branch**

SUBJECT: **Summary of Investigation and Review of Records and Reports associated with Donor Referral Services**

TO: **Paul Pierce, Special Agent, FDA Office of Criminal Investigations**

BACKGROUND

By authority of section 361 of the Public Health Service Act, the United States Food and Drug Administration (FDA) has regulated human tissue for transplantation into human recipients since 1993. Under section 361, FDA has made and enforced regulations necessary to prevent the introduction, transmission, or spread of communicable diseases within the States, between the States, or from foreign countries into the States. The regulations found at 21 CFR 1270 are applicable to human tissue recovered before May 25, 2005, while the regulations found at 21 CFR 1271 are applicable to human tissue recovered on or after May 25, 2005.[1]

HCT/Ps (human cells, tissues, and cellular and tissue-based products) recovered in one State, may be sent to another state for processing, then shipped for use throughout the United States, or beyond. A single donor may be the source of a large number of HCT/Ps. For example, a single long bone may be used to manufacture hundreds of HCT/Ps that may be implanted in just as many patients.

Certain diseases (known as relevant communicable diseases, or RCDs) are transmissible through the implantation, transplantation, infusion, or transfer of human cellular or tissue-based products derived from donors infected with those diseases. Currently, the following are considered by FDA as relevant communicable disease agents or diseases: HIV1/2 (Human Immunodeficiency Virus – the causative agents of Acquired Immunodeficiency Syndrome), Hepatitis B virus, Hepatitis C virus, human transmissible spongiform encephalopathy, including CJD (Creutzfeldt-Jakob disease, a fatal, degenerative brain disorder), and *Treponema pallidum*, the causative agent of syphilis. (See 21 CFR 1270.21 – communicable viruses, and 21 CFR 1271.3(r) and 1271.150(a) – relevant communicable diseases)

[1] See discussion of Legal Authority and rationale for promulgating the regulations found in 21 CFR 1271 at 69 FR 68613.

With very few exceptions, as noted later in this memorandum, people who have (or have ever had) these diseases are ineligible to donate tissues for implantation in others.

Donor Eligibility

In order to prevent the introduction, transmission, and spread of such diseases (RCDs), it is necessary to take appropriate measures to prevent the use of cells or tissues from infected donors. Thus, 21 CFR 1270.33(b)(1) and (2), and 12CFR 1271.45(b) require that before the use of most HCT/Ps, it must be determined whether the cell or tissue donor is eligible to donate. Donor Eligibility determination consists of two processes – donor testing and donor screening.

Currently there are no testing methods recognized by FDA or the scientific community that detect the presence of agents that cause RCDs in tissue itself. Therefore, testing is performed on the tissue donor's blood. Donor testing begins with collecting an appropriate[2] blood sample from the tissue donor. The blood sample is then tested for RCDs using available FDA licensed or cleared test kits. [21 CFR 1270.21(a)(b)(c) and 1271.80(a)]. A positive test result deems the donor ineligible for donation. The regulations at 1270 and 1271 do not allow an establishment to retest a donor who tests positive in an attempt to qualify the donor. The regulations are clear in both 1270 and 1271 that tissue recovered by an establishment such as Donor Referral Services and obtained from a donor who tests positive for a relevant communicable disease must not be used for implantation into a human patient.

When an individual first becomes infected with a virus, the body's immune system responds to the infection by producing antibodies to the virus. A number of tests for viral infection rely on detecting the antibody produced in response to the infection. It must be noted that there is a delay from the time of infection to the time there is enough antibody produced to be detected by any current tests.

When viruses infect an individual, there is also a delay from the time of infection to the time the virus replicates and spreads throughout the individual. Some tests for viral infection rely on detection of viral proteins. The number of viral proteins, however, needs to be at a high enough level in the individual for the test to be able to detect the infection.

The delay between infection and the ability to detect the infection (by either testing for the antibody produced in response to the infection, or testing for viral proteins) with the tests that are currently available is called the "window period". During the "window period", laboratory tests will not detect the infection and the individual may not even have exhibited early symptoms of infection, but the individual is capable of infecting others with the particular virus. There have been a number of instances identified where an individual was in the "window period", donated blood or tissue, and the recipients became infected with the virus.

[2] An appropriate sample for testing for RCDs is one that is properly labeled and can be related to the donor, contains the appropriate preservative, has been properly stored, and has not been diluted by infusion of fluids or transfusion of blood products. Often times prospective tissue donors may have been hospitalized prior to death, during which time they may have received medications or fluids through an intravenous line, or may have been transfused with a number of blood products. It is known that if the volume of infused fluids or transfused blood is large enough, it will result in a dilution (hemodilution) of the agents that are being tested for during laboratory testing for relevant communicable diseases. As a result a donor who is actually positive for one of the RCDs may test negative. In circumstances where donors have been hospitalized, the regulations require an assessment of the donor's hospital records to ensure that hemodilution has not occurred.

There are currently no tests for the disease agents that cause human TSE (transmissible spongiform encephalopathy, including Cruetzfeldt-Jakob disease (CJD). In layman's terms, TSE is an untreatable condition that results in total destruction of neurological systems. It is inevitably fatal. Because there is no test for the agents that cause this disease and because of the presence of a "window period" for other viral infections, it is a regulatory requirement that individuals who are tissue donors are screened for high risk behaviors. High risk behaviors are those that may place an individual at a higher risk of contracting a viral disease.

According to the regulations, tissue donor screening must include a review of relevant medical records, including but not limited to information from hospital records, coroner's offices, death certificates and, when performed, autopsy reports [21 CFR 1270.3(t) and 21 CFR 1271.3(s)].

Donor screening also includes a physical assessment [21 CFR 1270.3(n) and 1271.3(o)] of the donor for physical evidence of or risk factors for a RCD (e.g., track marks on the arms) as well as a documented interview with an individual or individuals who are able to provide a medical/social history of the donor [21 CFR 1270.3(h) and 1271.3(n)].

The purpose of the medical/social history is to determine if the donor engaged in behaviors or had a medical history that placed them at a higher risk for acquiring an RCD. An example of a "high risk" behavior is abuse of drugs injected with a needle in a non-medical environment, because sharing of needles has been shown to be a means of spreading communicable diseases (i.e. HIV, HBV, and HCV). An example of a medical history that may place an individual at a higher risk for acquiring an RCD is a medical condition, such as hemophilia that requires the long term, periodic use of blood products obtained from another individual. While the risk of transmission of a relevant communicable disease has been drastically decreased over the years in blood products necessary to counter the effects of hemophilia, there still remains an increased risk associated with this medical condition.

In most cases, a donor who tests reactive for a particular RCD, or who possesses clinical evidence of or risk factors for such a disease, would be considered ineligible, and cells and tissues from that donor would not ordinarily be used for transplantation into a human recipient.[3]

In addition to regulations governing the testing and screening of donors for relevant communicable disease and quarantine and storage of HCT/Ps, FDA has also determined that it is necessary to require HCT/P establishments to establish, follow and maintain written SOPs (standard operating procedures) to prevent the spread of relevant communicable diseases [21 CFR 1270.31, 21 CFR 1271.47, and 21 CFR 1271.180]. Examples of the SOPs FDA requires are written procedures for donor screening, donor testing, HCT/P processing and storage.

Federal regulations also require the manufacturer of HCT/Ps to maintain accurate, legible and indelible records related to the steps in manufacturing they perform [21 CFR 1270.33, 21 CFR 1271.55(d) and 21 CFR 2171.270]. Regulations, specifically 21 CFR 1270.33(f) and (h), 21 CFR 1271.270(d), and 21 CFR 1271.400 require these records to be maintained for 10 years and require that they be made available, upon request, to FDA investigators during the course of an inspection.

[3] None of the exceptions described at 21 CFR 1271.65(b) apply to the manufacturing steps Mr. Guyett was performing at his establishments in Nevada or in North Carolina.

Many HCT/Ps have a long shelf life. Additionally, as noted above, a donor may be a source of a large number of HCT/Ps. It may be discovered long after the donation and implantation has taken place that the donor tissue was infected and was capable of spreading an RCD. Should this occur, it would be necessary for the manufacturer to be able to retrieve unused, implicated tissue. In situations where implantation has occurred, it may be too late to prevent infections in the recipients, but it would not be too late for the recipient to obtain treatment and take steps to prevent infecting others.

For this reason, among others, FDA has determined that it is necessary to require HCT/P establishments to have in place a tracking system that assigns a distinct identifier to all HCT/Ps and associated records from a specific donor [21 CFR 1270.35 and 21 CFR 1271.290(c)]. These regulations require the ability to track an HCT/P from the donor to the consignee or final disposition, as well as from the consignee or final disposition to the donor.

Any establishment that engages in a manufacturing step (recovery, donor screening, donor testing, processing, storage or distribution of HCT/Ps) is required to comply with the regulations that are applicable to the manufacturing steps performed [21 CFR 1270.1(a) and 21 CFR 1271.150(c) (i)]. An establishment must have written SOPs for all manufacturing steps it performs, maintain records of manufacturing, and be able to determine where all HCT/Ps it manufactured are shipped. During an inspection by FDA of an establishment, these SOPs and records must be available for FDA to review.

DONOR REFERRAL SERVICES

Background

Mr. Philip Guyett has been registered with the FDA as the owner/president of a tissue establishment since 2004. First he was registered as the president of Donor Referral Services located at 3431 E. Sunrise Road, Suite 303-10, Las Vegas, NV from 2004-2005. Then, he was registered as the owner of Donor Referral Services, 4724 Hargrove Road, #182, Raleigh, North Carolina from 2005 to 2006.

A signed affidavit obtained by FDA investigators from Mr. Guyett on June 30, 2006 states that Mr. Guyett operated tissue recovery operations in both Nevada and North Carolina. In Mr. Guyett's affidavit he states that in addition to recovery of donors, he obtained medical history information from the next of kin, and that he also obtained a blood sample from the donor and submitted the sample to a laboratory for testing (for RCDs).

According to federal regulations (referenced above), Mr. Guyett manufactured HCT/Ps when he performed any or all steps in recovery, donor screening, and donor testing. Because Mr. Guyett was performing steps in the manufacture of HCT/Ps, he was required to comply with all federal regulations applicable to the specific manufacturing steps he performed. These regulations required the following:

1. Standard Operating Procedures for the steps in manufacturing he performed;

2. maintaining and retaining donor records for the steps in manufacturing he performed;

3. all records, including donor records generated by him, be accurate, indelible and legible;

4. the establishment of an identification system that assigned a unique donor identifier to each donor, so that all records and HCT/Ps related to that donor could be identified;

5. a tracking system that allows tracking of all HCT/Ps to the consignee; and

6. that the recovery organization (Mr. Guyett) determined whether pre-established criteria designed to prevent the transmission, introduction, or spread or RCDs had been met [21 CFR 1271.65(b)].

The processors[4] with whom Mr. Guyett did business were responsible for other steps in the manufacture of HCT/Ps including final donor eligibility determination prior to distribution of HCT/Ps for use in human patients. To make a final donor eligibility determination (determination that the use of the HCT/Ps would not result in or increase the risk of transmission of RCDs) the processors relied on the veracity of the manufacturing steps that Mr. Guyett had contracted with them to perform, and on the accuracy and truthfulness of the donor records and test results he provided to them for that purpose.

Inspection of DRS and FDA Enforcement Action

FDA conducted an inspection at the Raleigh, NC location of DRS. The inspection was conducted between June 28 and 30, 2006, and revealed that Philip Guyett had:

* failed to create and maintain accurate records of donor screening [21 CFR 1271.270(a)]; (There were no records of donor screening for any of the donors from whom Mr. Guyett recovered tissue.)

* failed to screen donors of cells or tissues by reviewing relevant medical records [21CFR 1271.75(a)]; (There were no records of the relevant medical records Mr. Guyett reviewed when he provided donor screening information to the processors.)

* failed to establish, maintain and follow appropriate procedures for all of the steps he performed in the manufacture of HCT/Ps [21 CFR 1271.47(a) and 1271.180(a)]; (Mr. Guyett had no written SOPs for the steps he performed in the manufacture of HCT/Ps.)

* failed to retain all records of donor recovery, screening and testing [21 CFR 1271.270(d)]; and, (There were no records of recovery, screening or testing for any of the donors from whom Mr. Guyett recovered tissue.)

[4] Processing is defined at 21 CFR 1270.3(p) and 21CFR1271.3(ff).

* failed to establish, maintain and follow standard operating procedures to assure that recovery of HCT/Ps took place in a suitable environment that would not cause contamination or cross-contamination during recovery, or increase the risk of the introduction, spread or communication of an RCD [21 CFR 1271.145, 21 CFR 1271.195(a)(2), and 21 CFR 1271.215].

Based on the violations of regulations listed above, and pursuant to 21 CFR 1271.440(a)(1) and (3), FDA ordered Mr. Guyett and Donor Referral Services to cease all manufacturing of HCT/Ps. The order was based on evidence collected during the June 2006 inspection regarding deviations from regulations found at 21 CFR 1271 (for tissue recovered on or after May 25, 2005).

These deviations represented a danger to the public health that necessitated immediate agency action to prevent Mr. Guyett and DRS from continuing to operate in a state of non-compliance. A copy of that order dated August 18, 2006 is attached. Upon issuance of the order for cessation, FDA continued to investigate Mr. Guyett's operations prior to May 25, 2005 to ascertain the full scope of the violations committed by Mr. Guyett and the potential impact of those violations on the health of recipients of distributed HCT/Ps that were processed from human tissue recovered by Mr. Guyett.

Investigation of DRS by FDA

The inspection summarized above found that Mr. Philip Guyett had maintained no written SOPs for the steps he performed in the recovery, donor screening and donor testing of HCT/Ps, and he had maintained no records of donor screening, testing or recovery for any of the HCT/Ps he had sent to the processors with whom he had contracts. Mr. Guyett had failed to maintain a tracking system that enabled tracking of the HCT/P to the consignee (the processor), however, Mr. Guyett did provide an affidavit containing the names of the processors he recalled doing business with.

Because Mr. Guyett did not have any of the records he was required to maintain, FDA's investigation of DRS could only be accomplished by performing inspections of the processors that Mr. Guyett did business with to obtain copies of the donor records that he had shipped to them with the recovered tissues. The donor records Mr. Guyett shipped to the processors are the records that the processors used to make a final donor eligibility determination prior to release of the HCT/Ps for use in a human recipient.

FDA conducted inspections of the testing laboratories noted below to obtain "test of record"[5] results for RCD testing maintained by those laboratories. Additionally, site visits were performed by FDA investigators at various funeral homes with whom Mr. Guyett had arrangements for recovery of HCT/Ps. Site visits were also performed at the appropriate state agencies to obtain certified death certificates containing relevant medical information for the donors recovered by Mr. Guyett.

FDA's Center for Biologics Evaluation and Research received and reviewed all reports, documents, and records associated with the FDA investigation of operations of DRS (Donor Referral Services), and Mr. Philip J. Guyett, Owner and Director of DRS. These reports, documents and records include the following:

[5] "Test of record" refers to the testing records and results of testing required by FDA to be maintained by the laboratory. The results of these tests are the results that FDA requires to be used for donor eligibility determination.

* EIRs (Establishment Inspection Reports) for inspections conducted at DRS, Raleigh, NC; ATS, San Antonio, TX; USCT (now owned by Allosource Tissue, Cincinnati, OH); LMTB; Kennesaw, GA; Laboratories at Bonfils, Aurora CO; Viromed Laboratories, Minnetonka, MN; Consolidated Laboratory Services, Las Vegas, NV; and, a number of funeral homes located in Raleigh, NC and in the Las Vegas, NV areas.

* Original death certificates for donors recovered by DRS at both the Raleigh, NC and Las Vegas, NV locations.

* Copies of "test of record" laboratory testing records for all donors recovered by DRS at both the Raleigh, NC and Las Vegas, NV locations provided by the testing laboratories (Viromed, Minnetonka, MN; Laboratories at Bonfils, Aurora, CO and Consolidated Laboratory Services, Las Vegas, NV).

* Summaries provided by Laboratories at Bonfils related to their internal investigation of test record discrepancies related to donors F05-01, E05-07, E05-06, and E05-03.

* Affidavits obtained from Mr. Philip J. Guyett and affidavits obtained from directors of funeral homes in the Las Vegas, NV and Raleigh, NC areas.

* Information obtained from obituaries found during an internet search of relevant news papers for donors recovered by DRS at the NV and NC locations.

SUMMARY OF VIOLATIONS IMPACTING THE PUBLIC HEALTH

Mr. Guyett told FDA investigators on June 30, 2006 that he had established a system to assign a donor number to each HCT/P donor from whom he recovered HCT/Ps. This system was explained as follows: the first character of the donor number is alpha and represents the month in which the donor was recovered, for example A=January; B=February, etc. The next two characters are numeric and represent the last two digits of the year in which the recovery took place, for example 04 = 2004, 05=2005, etc. The last two characters are numeric and represent the chronological order of the donor in relation to others recovered in that specific month and year, for example, 01=first donor recovered in the month and year represented by the preceding characters, 02=the second donor, etc. With the exception of two donors for whom traceability was lost by DRS, I have used the DRS identification numbers in the summary below. The two donors for whom Mr. Guyett failed to maintain traceability are discussed in Item 1 below. The initials of the first donor are BHD. The initials of the second donor discussed in item 1 below are HJS.

Copies of at least one hundred DRS donor records were obtained collectively from the processors. The review of records was performed by comparing "test of record" reports obtained from the relevant testing laboratory to the test record Mr. Guyett had included in the donor records he provided to the respective processor. Additionally, the certified death certificate was compared to the donor screening information provided by Mr. Guyett in the donor records he provided to the respective processor. The following significant differences were found to exist between "test of record" results on file with the respective testing laboratory and/or medical information found on certified death certificates and the results of donor screening and testing that Mr. Guyett represented to the respective processor as being complete, accurate and truthful.. These examples represent Mr. Guyett's most egregious violations of the regulations, and his

flagrant disregard for the health of the eventual recipients of HCT/Ps recovered by Donor Referral Services.

1. Falsification of Test Results for Relevant Communicable Disease and Donor Screening information

Donor BHD

The certified death certificate obtained by FDA from the North Carolina department of vital statistics states the cause of death of donor BHD was cardiopulmonary arrest as a consequence of hepatacellular carcinoma (liver cancer) with metastases (cancer had spread to other organs) and liver cirrhosis secondary to chronic Hepatitis C. The death certificate states that Hepatitis C infection was a significant condition contributing to the donor's death. The information in the certified death certificate alone is significant enough to deem donor BHD as ineligible for donation of HCT/Ps for implantation in a human recipient.

Mr. Pierce, you related to me that during an interview you conducted with Mr. Guyett, he told you that he was aware of the fact this donor had a history of Hepatitis C, a factor that would cause the donor to be ineligible for HCT/P donation. During the same interview Mr. Guyett told you that he received testing results from LABS and that donor BHD tested positive for Hepatitis C. Mr. Guyett related to you that he held the tissue he recovered from donor BHD in storage until he received negative test results for a different donor he had recovered after donor BHD. Mr. Guyett told you he then submitted a blood sample he had retained from the donor who had tested negative, but identified the blood sample has having been obtained from donor BHD.

My review of the "test of record" results obtained from LABS found evidence that corroborates what Mr. Guyett told you during your interview with him. Review of LABS test of records found that Mr. Guyett had originally submitted a blood sample for donor BHD identified as C05-06. The test of record results from LABS document that the blood sample tested positive for Hepatitis C. LABS had a second test record containing the same donor identification information as donor BHD (date of death, age, etc). That test record identified the blood sample as D05-02, and indicates negative test results for all relevant communicable diseases.

Mr. Pierce, you also related to me that during the interview you conducted with Mr. Guyett, he told you that often he did not actually conduct a face to face interview regarding medical history/behavior with the next of kin. Mr. Guyett told you that instead, he would complete the donor screening record to make it appear that he had questioned the next of kin about the donor's medical history/behavior, and would complete the donor screening record to give the appearance that the donor was eligible to donate HCT/Ps. Alternatively, Mr. Guyett told you that if he actually did talk to the next of kin and the next of kin provided information that would deem the donor ineligible, Mr. Guyett would omit that information from the donor screening record.

My record review corroborates the information Mr. Guyett provided to you during your interview with him. In the records Mr. Guyett presented to the processor, he stated the cause of death was a heart attack, and he stated the answer to the following medical history/behavior questions was NO:

> * Has the donor suffered from any type of liver disease or ever been told they had any type of Hepatitis? (a yes answer would disqualify the donor)

* Has the potential donor been seen by any physicians, institutionalized, or hospitalized in the past 2 years?
* Did the potential donor have any serious illnesses?
* Has the potential donor ever had cancer?"

Based on the factual information regarding this donor, all of these questions should have been answered YES.

Summary – Mr. Guyett falsified donor testing records as well as donor screening records to make this donor appear to be eligible for donation of HCT/Ps. The tissue processor, USCT, is not required by FDA regulations to perform additional donor screening or testing[6], but relied on the integrity and accuracy of the information Mr. Guyett presented to make a donor eligibility determination. Mr. Guyett falsified donor testing records, failed to accurately document donor medical history/behavior, and presented donor BHD to the processor as having no disqualifying criteria. Additionally, the alterations that Mr. Guyett made to the records for donor BHD were made in a way that would not be detected by the processor during review.

Mr. Guyett shipped tissue from donor BHD to USCT. Based on the falsified records provided by Mr. Guyett, USCT found this donor to be eligible. As of this date, 35 HCT/Ps processed from donor BHD had been distributed. Nine HCT/Ps were distributed to foreign customers, and 26 HCT/Ps were distributed domestically (Springfield, MA; San Jose, CA; Williston, ND; Stafford, AZ; and, Reno, NV). Records document that, of the nine HCT/Ps distributed to foreign customers, 2 HCT/Ps were distributed to a customer in Ankara, Turkey and were implanted. Records document that the remaining 7 HCT/Ps in foreign distribution were sent to a customer in Ioannina, Greece and were implanted. Of the remaining 26 HCT/Ps distributed domestically[6], were implanted.

2. Falsification of Test Results for Relevant Communicable Diseases

Donor HJS

My review of LABS test of record results found that Mr. Guyett substituted a blood sample known by him to be negative for all relevant communicable diseases for donor HJS in the same manner as he did for donor BHD. Review of LABS test of records found that Mr. Guyett had originally submitted a blood sample for donor HJS identified as D05-01. The test of record results document blood sample D05-01 tested positive for Hepatitis B core antibody, indicating a past infection with Hepatitis B, and document the blood sample also tested positive by a screening test for syphilis.
LABS had a second test of record containing the same donor identification information as donor HJS (age, date of death, etc). That second test record identified the blood samples as D05-03, and indicated negative test results for all relevant communicable diseases.

Summary – Mr. Guyett falsified donor testing records to make this donor appear to be eligible for donation of HCT/Ps. The tissue processor, USCT, is not required by FDA regulations to perform additional donor screening or testing[7], but relied on the integrity and accuracy of the information Mr. Guyett presented to make a donor eligibility determination. Mr. Guyett presented donor HJS to USTS as having no disqualifying criteria.

[6] The regulations specifically prohibit additional testing for relevant communicable diseases to qualify a donor once a blood sample from the donor tests positive for HIV-1/2, Hepatitis B, or Hepatitis C.

The falsification of test records for donor HJS by Mr. Guyett were made in a way that would not be detected by the processor during review.

Mr. Guyett shipped tissue from HJS to USCT. Based on the falsified records provided by Mr. Guyett, USCT determined the donor to be eligible and processed the tissue into HCT/Ps which were distributed for implantation into human recipients by TissueNet, Orlando, FL. TissueNet initiated customer notification of HCT/PS manufacture from HJS on July 10, 2006.

As of that time, 5 HCT/Ps processed from HJS had been distributed. Three HCT/Ps were distributed to a foreign customer in Vancouver, BC. Records document these HCT/PS had not been implanted and were returned to TissueNet. Two HCT/Ps were distributed domestically to customers in Melbourne, FL and Oklahoma City, OK. Records document both of those HCT/PS were implanted.

DRS Donors E05-03, E05-06, E05-07, F05-01, and F05-02

The results of testing for RCDs in each of these five donors' presented by Mr. Guyett to the respective processors (USCT for donors E05-03, E05-06, E05-07; LMTB for donor F05-01; and, ATS for donor F05-02) indicate that each donor tested negative for all tests. The test of record results from LABS document that each of these donors tested positive for Hepatitis B core antibody, indicating a previous infection with Hepatitis B. As noted previously, this is a condition that would disqualify these donors from donating tissues for implantation into human recipients, and which if known by the processor would have resulted in rejection of the donor's tissue.

I communicated differences in records noted above to the respective processors. LMTB requested LABS to perform an investigation regarding records for donor F05-01. LABS sent me a written summary of the results of their investigation, which concluded that the test of record was altered to reflect negative test results after it was sent to Mr. Guyett and before Mr. Guyett sent the test result to LMTB.

Summary – Mr. Guyett falsified the test results for these five donors. Apparently this was accomplished by "cutting" the disqualifying test results from the test records and "pasting" acceptable results into the test records. In this way Mr. Guyett presented records to the respective processor that made the donor appear to be eligible, when in fact, if the true test results had been known by the processor, the donor would have been disqualified.

DRS Donor E04-11

My review of records for this donor found that the testing laboratory, in this case Viromed, tested a blood sample for this donor for all relevant communicable diseases, but were unable to perform a test for HIV for this donor because no sample was received from Mr. Guyett for that test. Inexplicably, Mr. Guyett was able to produce a second sample of blood from this donor and submitted the sample to Viromed for HIV testing. It is virtually impossible that the second blood sample was actually obtained from donor E04-11, as the first blood sample was found to be blood group O. The second sample Mr. Guyett produced was found to be blood group A.

Summary –It is likely that Mr. Guyett had no reserve blood sample from this donor, so to be able to give the appearance of the donor being eligible, Mr. Guyett submitted a blood sample

from some unknown source to Viromed for HIV testing.

3. Falsification of Donor Screening for Clinical Signs of or Risk Factors for Relevant Communicable Disease(s)

The importance of donor screening has been explained above. When a comparison was made of medical information documented on certified death certificates and the information Mr. Guyett provided to the processor the following discrepancies were found:

DRS Donor E04-11

The certified death certificate for DRS donor E04-11 states the donor died of methadone and opiate intoxication in a hotel room in Las Vegas, NV. The death certificate also states that an autopsy was performed.

Mr. Guyett falsely represented the cause of death for this donor as "a collapse at home, DOA". Additionally, any donor behavior questions addressing the use of illicit drugs were answered as NO in the records Mr. Guyett provided to the processor.

Summary – The donor screening records for donor E04-11 provided by Mr. Guyett to the processor do not include the cause of death stated in the certified death certificate, drug overdose, a circumstance that would call into question whether the donor had risk factors (IV drug use) for RCDs, and for which the processor would have disqualified the donor. Additionally, an autopsy report is considered by FDA regulations to be a relevant medical record. Those same regulations state that if an autopsy is performed, and if a copy is available, the autopsy report must be reviewed as part of the donor screening process. Mr. Guyett failed to obtain a copy of the autopsy report for this donor.

DRS Donor G05-03

The certified death certificate for this donor states the cause of death was cancer, with other contributing factors, including drug addiction and IV drug abuse.

The donor screening information contained in the records provided by Mr. Guyett to the processor, ATS includes a copy of a death certificate altered by Mr. Guyett to state the cause of death for this donor was ASCVD (atherosclerotic cardio vascular disease) with other contributing factors, including emphysema and tobacco abuse. Additionally, any questions addressing the use of IV drugs were answered as NO in the records Mr. Guyett provided to the processor.

Summary –Mr. Guyett falsified the death certificate he provided to ATS for donor G05-03 by deleting any information that would cause the processor to disqualify the donor.

4. Blood Sample for Laboratory Testing for Relevant Communicable Disease(s) not Properly Assessed for Hemodilution

As previously explained the accuracy of the testing for RCDs is dependant on an appropriate sample. An appropriate sample for testing for RCDs is one that is properly labeled, contains the appropriate preservative, has been properly stored, and has not been diluted by infusion of fluids

or transfusion of blood products. Often times prospective tissue donors may have been hospitalized prior to death, during which time they may have received medications or fluids through an intravenous line, or may have been transfused with a number of blood products. It is known that if the volume of infused fluids or transfused blood is large enough, it will result in a dilution (hemodilution) of the agents that are being tested for during laboratory testing for relevant communicable diseases. As a result a donor who is actually positive for one of the RCDs may test negative. In clinical situations where donors may have received fluids or blood products intravenously, i.e. during hospitalization, the regulations [21 CFR 1270.21 (h)(2) and 21 CFR 1271.80(d) require an assessment of the donor's medical hospital records to ensure that hemodilution has not occurred.

A review of the certified death certificates for two of the donors from whom Mr. Guyett recovered HCT/Ps were inpatients [death certificates state INPATIENT as opposed to choices of DOA or ER patient] of a medical facility prior to death. The DRS identification numbers for these donors are: G04-09 and D05-05.

Summary - A review of the donor records provided by Mr. Guyett to the respective processors found Mr. Guyett provided no information regarding the fact the donor was an inpatient of a hospital prior to death. There is an assessment form for hemodilution included in each DRS donor record for these two donors. However, there is no evidence that the donor's hospital records were adequately reviewed for documentation of infusion or transfusion, and that an appropriate assessment was made of the blood sample used for testing for RCDs.

5. Contractual Agreements/Other Inaccuracies found in Donor Screening Records

During its investigation of DRS, FDA obtained copies of each contract that had been signed by Philip Guyett and the respective tissue processor[4] (USCT, U.S. Cell and Tissue; ATS, Alamo Tissue Services; and LMTB, Lost Mountain Tissue Bank). Each contract confirms what Mr. Guyett stated in his affidavit, that he recovered tissue, performed donor screening, obtained from the donor a blood sample and submitted the blood sample to a laboratory for testing for RCDs.

Two of the contracts state that Mr. Guyett would receive the records of results of testing for RCDs and ship those testing records to the respective processor (USCT and ATS). The contract with ATS states that Mr. Guyett would provide to ATS a copy of the donor's death certificate and if performed, a report of the autopsy. The contracts specify that Mr. Guyett would conduct all of his operations in accordance with Federal Regulations of the FDA and the standards of AATB (the American Association of Tissue Banks[6]), and that he would screen donors according to acceptance criteria established by the processor, in accordance with FDA regulations and AATB standards.

[6] AATB is an acronym for the HCT/P industry organization, American Association of Tissue Banks. This organization grants accreditation to establishments and to individuals who meet a written set of standards. Included in this set of written standards are donor criteria that are more specific than the requirements established by Federal regulations. For example, the 10th Edition of AATB standards printed in 2002 states that tissue from a donor who exhibits significant active infection, including septicemia should not be used for implantation into another recipient. Those standards also recommend exclusion of donors with a history of dementia or degenerative neurological disorders. Finally, the standards recommend exclusion of donors with a history cancer, but, delegate the final responsibility and decision regarding these donors to the medical director of the firm that would be making a final donor eligibility determination.

Review of records provided by Mr. Guyett to the respective processor and comparison of those records to certified death certificates found that Mr. Guyett did not provide an accurate record of the donor's medical/social history because to do so likely would have resulted in disqualification by the processor:

* The certified death certificates for 25 donors state the cause of death or a contributing factor to the donor's death was some form of cancer. However, in the records provided by Mr. Guyett to the respective processors for each of these donors, Mr. Guyett states a cause of death other than cancer or malignancy. Additionally, on the medical assessment form that he utilized to document the donor medical history interview, Mr. Guyett indicated a NO answer to the question regarding cancer or malignant disease. The DRS identification numbers for these donors are: D04-02, E04-02, E04-12, F04-07, G04-05, H04-01, I04-02, I04-03, J04-05, K04-01, L04-05, L04-06, L04-09, A05-05, B05-03, C05-01, D05-03, D05-04, E05-04, E05-09, F05-01, F05-03, G05-03, K05-04.

* The certified death certificates for 6 donors state the cause of death or a contributing factor to the donor's death was dementia and/or Alzheimer's disease. However, in the records provided by Mr. Guyett to the respective processors for each of these donors, Mr. Guyett states a cause of death other than dementia or Alzheimer's. Additionally, on the medical assessment form that he utilized to document the donor medical history, Mr. Guyett indicated a NO answer to the question regarding dementia or Alzheimer's disease. The DRS identification numbers for these donors are: G04-02, I04-01, L04-08, C05-03, E05-07, and F05-02.

* The certified death certificates for 2 donors states the cause of death or a contributing factor to the donor's death was septicemia/sepsis (a condition indicating widespread bacterial infection). However, in the records provided by DRS to the respective processors for each of these donors, Mr. Guyett states a cause of death other than infection, sepsis or septicemia. Additionally, on the medical assessment form that Mr. Guyett utilized to document the donor medical history interview, he indicated a NO answer to the question regarding infection, septicemia, or sepsis. The DRS identification numbers for these donors are: J04-07 and J04-09.

DRS records for three donors failed to accurately document more than one medical condition that would have resulted in disqualification by the processor as follows:

K04-02
The certified death certificate for this donor states the cause of death was sepsis, and also states the donor had dementia.

L04-01
The certified death certificate for this donor states the cause of death was severe sepsis, fulminant hepatic failure (sudden and severe liver failure), and metastatic prostate cancer.

L04-12
The certified death certificate states the causes of death as septic shock, staph infection, UTI (urinary tract infection), and dementia.

Summary - Regulations at 21 CFR 1270.33(a) and at 21 CFR 1271.270(a) require records to be accurate. The donor records noted above represent thirty seven examples of Mr. Guyett's failure to provide accurate donor medical history information to the processors with whom he had contractual agreements. The donor records also represent thirty seven examples of Mr. Guyett's failure to fulfill the requirements of his contractual agreements with the processors to observe and follow standards and donor criteria established by the American Association of Tissue Banks.[6]

CONCLUSION OF SUMMARY INFORMATION

To carry out its vast responsibility of protecting the health and well being of the American public, FDA is authorized to make and enforce regulations that are necessary to prevent the introduction, transmission, or spread of communicable diseases. The regulations at 21 CFR 1270 and 21 CFR 1271 are designed to prevent the introduction, transmission, or spread of communicable diseases through the use of human tissue recovered and processed for implantation into human recipients.

Those regulations specifically prohibit the implantation of HCT/Ps recovered from a donor who tests positive for a communicable disease, or who exhibited clinical signs of or behavior at risk for a communicable disease. Additional regulations outline specific requirements for each step in manufacturing to ensure that such HCT/Ps will not be used for implantation into a human recipient.

In the course of conducting business as DRS, Mr. Philip Guyett performed steps in the manufacture of HCT/Ps for implantation in human recipients. As such, DRS and Mr. Guyett were subject to FDA regulations found at 21 CFR 1270 (tissue recovered prior to May 25, 2005) and at 21 CFR 1271 (tissue recovered on or after May 25, 2005).

Based on my review of the records, Mr. Guyett violated a significant number of regulations designed to prevent the introduction, transmission, or spread of communicable diseases. These violations resulted in the distribution of HCT/Ps that represent a significant risk to the health of the American public.

Of the 100 donor records reviewed, approximately half of them (48) contained omissions, deletions, or alterations of information that if known, would cause the processor to deem the donor ineligible. The violations noted in this summary only represent those that could be identified by a review of records . Mr. Guyett may have committed other violations that a review of records would not identify. Therefore, FDA has no assurance that any of the tissue recovered by Mr. Guyett from the 100 donors was suitable for implantation into a human recipient.

Records from each of the processors document that approximately 2,600 HCT/Ps manufactured from tissue provided to them by Mr. Guyett were distributed in domestic and foreign commerce. Of that number, at least 785 were implanted into human recipients.

As noted earlier, implantation of HCT/Ps not manufactured in accordance with Federal Regulations poses a risk of introduction, transmission, or spread of communicable diseases in the recipient, and poses a risk of infection of others by the recipient.

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